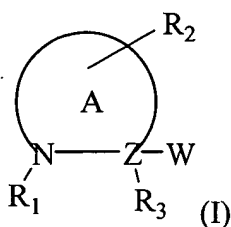


In the claims:

1-3. (Cancelled)

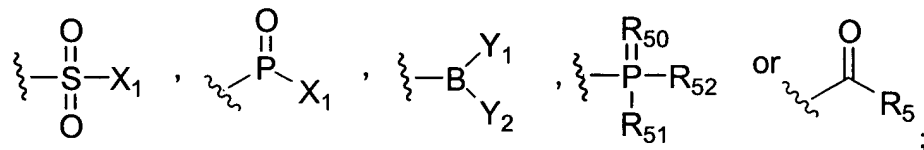
4. (Currently amended) A method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) represented by Formula I in an amount sufficient to treat Type II diabetes but not sufficient to suppress the immune system of the animal:



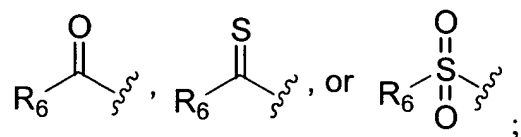
wherein

A represents a 4-8 membered heterocycle including the N and a C α carbon;

Z represents C or N;

W represents -CH=NR₅,

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C- terminally linked peptide or peptide analog, or an amino-protecting group, or



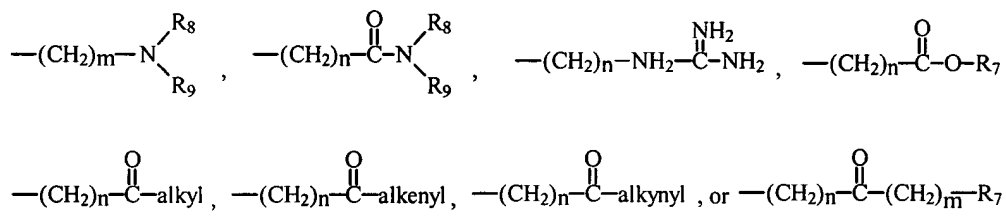
R₂ is absent or represents one or more substitutions to the ring A, each of which can

independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

if Z is N, R₃ represents hydrogen, if Z is C, R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₅ represents a hydrogen, an alkyl, an alkenyl, an alkynyl, -C(X₁)(X₂)X₃, -(CH₂)_m-R₇, -(CH₂)_n-OH, -(CH₂)_n-O-alkyl, -(CH₂)_n-O-alkenyl, -(CH₂)_n-O-alkynyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_n-SH, -(CH₂)_n-S-alkyl, -(CH₂)_n-S-alkenyl, -(CH₂)_n-S-alkynyl, -(CH₂)_n-S-(CH₂)_m-R₇, -C(O)C(O)NH₂, or -C(O)C(O)OR'₇;

R₆ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-alkyl, -(CH₂)_m-O-alkenyl, -(CH₂)_m-O-alkynyl, -(CH₂)_m-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-alkyl, -(CH₂)_m-S-alkenyl, -(CH₂)_m-S-alkynyl, or -(CH₂)_m-S-(CH₂)_m-R₇,



R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R'₇ represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocycle;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, -(CH₂)_m-R₇, -C(=O)-alkyl, -C(=O)-alkenyl, -C(=O)-alkynyl, or -C(=O)-(CH₂)_m-R₇,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₅₀ represents O or S;

R₅₁ represents N₃, SH, NH₂, NO₂ or OR'₇;

R₅₂ represents hydrogen, a lower alkyl, an amine, OR'7, or a pharmaceutically acceptable salt, or R₅₁ and R₅₂ taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

Y₁ and Y₂ can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

X₁ represents a halogen;

X₂ and X₃ each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

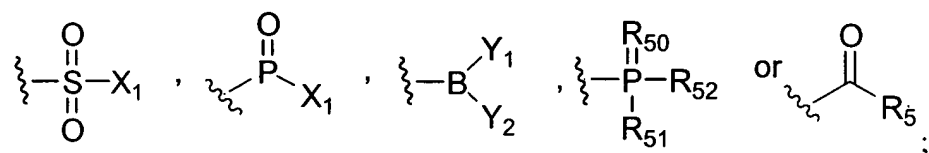
5. (Currently amended) The method of claim ~~1 or 24~~, wherein the animal is a mammal.
6. (Currently amended) The method of claim ~~54~~, wherein the mammal is a human.
7. (Cancelled)
8. (Currently amended) The method of claim ~~1, 2, 3 or 4~~, wherein the inhibitor has an EC₅₀ for modification of glucose metabolism which is at least one order of magnitude less than its EC₅₀ for immunosuppression.
9. (Currently amended) The method of claim ~~1, 2, 3 or 4~~, wherein the inhibitor has an EC₅₀ for inhibition of glucose intolerance in the nanomolar or less range.
10. (Previously presented) The method of claim 8, wherein the inhibitor has an EC₅₀ for immunosuppression in the micromolar or greater range.
11. (Currently amended) The method of claim 4, or 6, wherein the inhibitor has a K_i for DPIV inhibition of 1.0 nM or less.
12. (Currently amended) The method of claim ~~1, 2, 3 or 4~~, wherein the inhibitor is peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala.

13. (Currently amended) The method of claim ~~1, 2, 3 or 4~~, wherein the inhibitor has a molecular weight less than 7500 amu.

14. (Currently amended) The method of claim ~~1, 2, 3 or 4~~, wherein the inhibitor is administered orally.

15. (Cancelled)

16. (Currently amended) The method of claim ~~1, 2, 3, or 4~~, wherein W represents $-\text{CH}=\text{NR}_5$,



R_5 represents H, an alkyl, an alkenyl, an alkynyl, $-\text{C}(\text{X}_1)(\text{X}_2)\text{X}_3$, $-(\text{CH}_2)_m-\text{R}_7$, $-(\text{CH}_2)_n-\text{OH}$, $-(\text{CH}_2)_n-\text{O-alkyl}$, $-(\text{CH}_2)_n-\text{O-alkenyl}$, $-(\text{CH}_2)_n-\text{O-alkynyl}$, $-(\text{CH}_2)_n-\text{O}-(\text{CH}_2)_m-\text{R}_7$, $-(\text{CH}_2)_n-\text{SH}$, $-(\text{CH}_2)_n-\text{S-alkyl}$, $-(\text{CH}_2)_n-\text{S-alkenyl}$, $-(\text{CH}_2)_n-\text{S-alkynyl}$, $-(\text{CH}_2)_n-\text{S}-(\text{CH}_2)_m-\text{R}_7$, $-\text{C}(\text{O})\text{C}(\text{O})\text{NH}_2$, or $-\text{C}(\text{O})\text{C}(\text{O})\text{OR}'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

Y_1 and Y_2 can independently or together be a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y_1 and Y_2 are connected via a ring having from 5 to 8 atoms in the ring structure;

R_{50} represents O or S;

R_{51} represents N_3 , SH, NH_2 , NO_2 or OR'_7 ;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7 , or a pharmaceutically acceptable salt, or R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

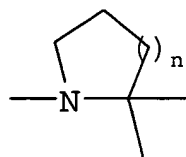
X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

m is zero or an integer in the range of 1 to 8; and

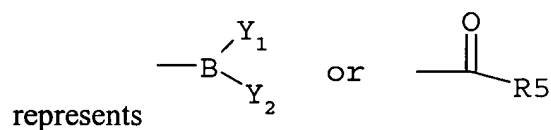
n is an integer in the range of 1 to 8.

17. (Previously presented) The method of claim 16, wherein the ring A is represented by the formula:

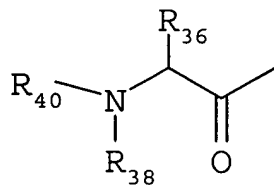


wherein n is an integer of 1 or 2.

18. (Previously presented) The method of claim 16, wherein W



19. (Original) The method of claim 16, wherein R_1 represents



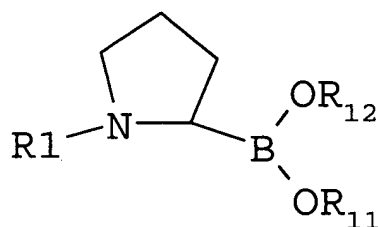
R_{36} is a small hydrophobic group and R_{38} is hydrogen, or, R_{36} and R_{38} together form a 4-7

membered heterocycle including the N and the $C\alpha$ carbon, as defined for A above; and

R_{40} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group.

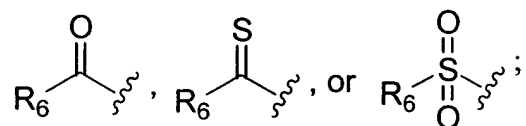
20. (Previously presented) The method of claim 16, wherein R_2 is absent, or represents a small hydrophobic group.

21. (Previously presented) The method of claim 16, wherein R_3 is a hydrogen, or a small hydrophobic group.
22. (Previously presented) The method of claim 16, wherein R_5 is a hydrogen, or a halogenated lower alkyl.
23. (Previously presented) The method of claim 16, wherein X_1 is a fluorine, and X_2 and X_3 , if halogens, are fluorine.
24. (Currently amended) The method of claim 16, wherein the inhibitor is represented by the general formula:



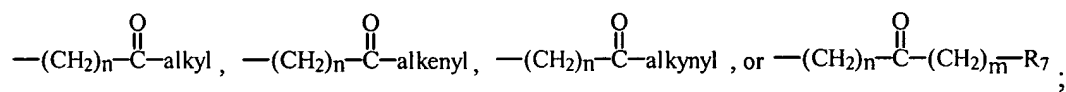
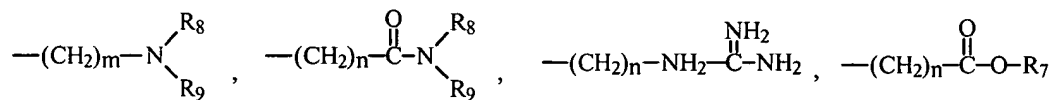
wherein

R_1 represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or



R_6 represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, -

$(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, -
 $(CH_2)_m-S-(CH_2)_m-R_7$,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

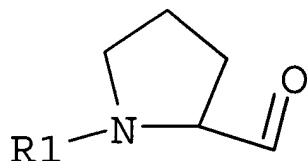
R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, $-(CH_2)_m-R_7$, $-C(=O)-alkyl$, $-C(=O)-alkenyl$, $-C(=O)-alkynyl$, or $-C(=O)-(CH_2)_m-R_7$,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

R₁₁ and R₁₂ each independently represent ~~hydrogen~~, an alkyl, or a pharmaceutically acceptable salt, or R₁₁ and R₁₂ taken together with the O-B-O atoms to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

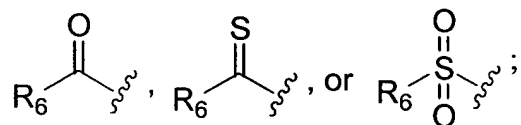
m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

25. (Previously presented) The method of claim 16, wherein the inhibitor is represented by the general formula

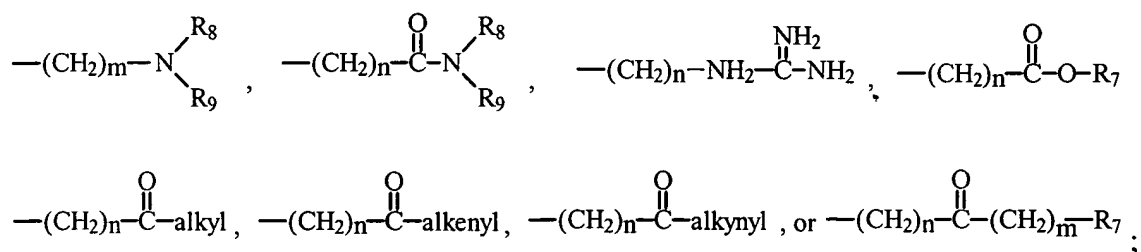


wherein

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or



R₆ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O-alkyl$, $-(CH_2)_m-O-alkenyl$, $-(CH_2)_m-O-alkynyl$, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S-alkyl$, $-(CH_2)_m-S-alkenyl$, $-(CH_2)_m-S-alkynyl$, $-(CH_2)_m-S-(CH_2)_m-R_7$,



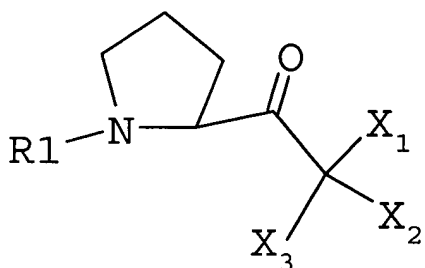
R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, $-(\text{CH}_2)_m-\text{R}_7$, $-\text{C}(=\text{O})-\text{alkyl}$, $-\text{C}(=\text{O})-\text{alkenyl}$, $-\text{C}(=\text{O})-\text{alkynyl}$, or $-\text{C}(=\text{O})-(\text{CH}_2)_m-\text{R}_7$,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

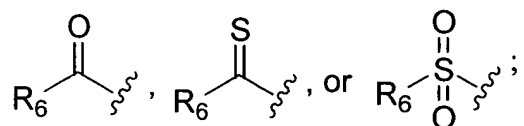
m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

26. (Currently amended) The method of claim 16, wherein the inhibitor is represented by the general formula:



wherein

R₁ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino protecting group, or

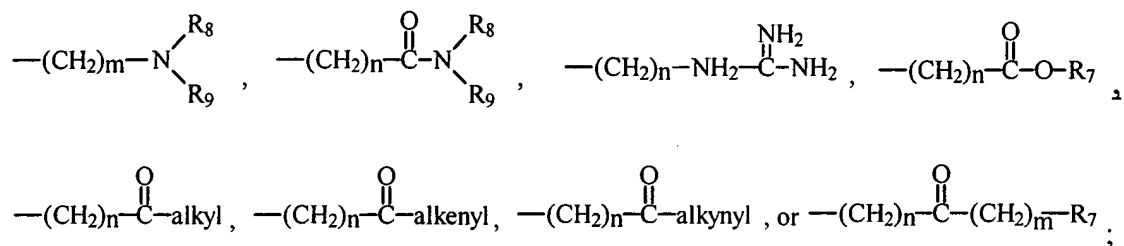


R₆ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(\text{CH}_2)_m-\text{R}_7$, -

$(\text{CH}_2)_m-\text{OH}$, $-(\text{CH}_2)_m-\text{O}-\text{alkyl}$, $-(\text{CH}_2)_m-\text{O}-\text{alkenyl}$, $-(\text{CH}_2)_m-\text{O}-\text{alkynyl}$, $-(\text{CH}_2)_m-\text{O}-$

$(\text{CH}_2)_m-\text{R}_7$, $-(\text{CH}_2)_m-\text{SH}$, $-(\text{CH}_2)_m-\text{S}-\text{alkyl}$, $-(\text{CH}_2)_m-\text{S}-\text{alkenyl}$, $-(\text{CH}_2)_m-\text{S}-\text{alkynyl}$, -

$(\text{CH}_2)_m-\text{S}-(\text{CH}_2)_m-\text{R}_7$,



R₇ represents an aryl, a cycloalkyl, a cycloalkenyl, or a heterocycle;

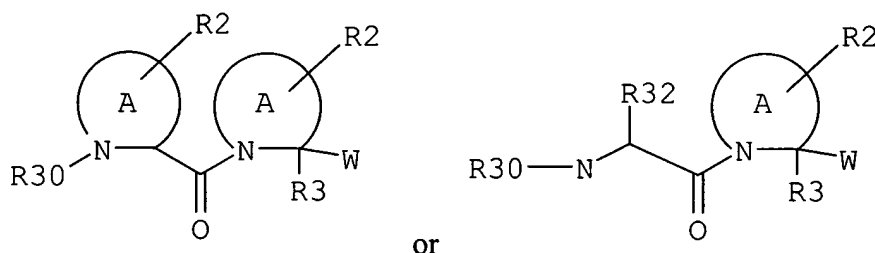
R₈ and R₉ each independently represent hydrogen, alkyl, alkenyl, $-(\text{CH}_2)_m-\text{R}_7$, $-\text{C}(=\text{O})-\text{alkyl}$, $-\text{C}(=\text{O})-\text{alkenyl}$, $-\text{C}(=\text{O})-\text{alkynyl}$, or $-\text{C}(=\text{O})-(\text{CH}_2)_m-\text{R}_7$,

or R₈ and R₉ taken together with the N atom to which they are attached complete a heterocyclic ring having from 4 to 8 atoms in the ring structure;

X₁, X₂ and X₃ each represent a halogen;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

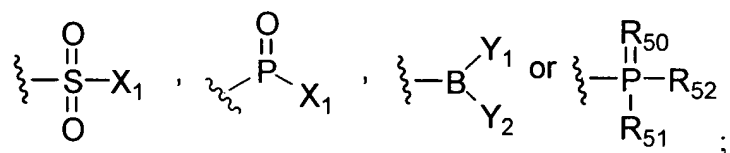
27. (Previously presented) The method of claim 16, wherein the inhibitor is represented by the general formula:



wherein

A represent a 4-8 membered heterocycle including an N and a C α carbon;

W represents,



R₂ is absent or represents one or more substitutions to the ring A, each of which can

independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(\text{CH}_2)_m-\text{R}_7$, $-(\text{CH}_2)_m-\text{OH}$, $-(\text{CH}_2)_m-\text{O-lower alkyl}$, -

$(\text{CH}_2)_m\text{-O-lower alkenyl}$, $-(\text{CH}_2)_n\text{-O-(CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_m\text{-SH}$, $-(\text{CH}_2)_m\text{-S-lower alkyl}$, $-(\text{CH}_2)_m\text{-S-lower alkenyl}$, or $-(\text{CH}_2)_n\text{-S-(CH}_2)_m\text{-R}_7$;

R_3 represents a hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_m\text{-OH}$, $-(\text{CH}_2)_m\text{-O-lower alkyl}$, $-(\text{CH}_2)_m\text{-O-lower alkenyl}$, $-(\text{CH}_2)_n\text{-O-(CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_m\text{-SH}$, $-(\text{CH}_2)_m\text{-S-lower alkyl}$, $-(\text{CH}_2)_m\text{-S-lower alkenyl}$, or $-(\text{CH}_2)_n\text{-S-(CH}_2)_m\text{-R}_7$;

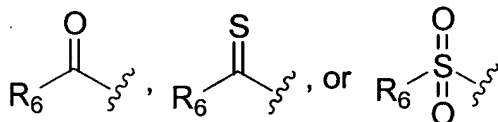
R_5 represents a hydrogen, an alkyl, an alkenyl, an alkynyl, $-\text{C}(\text{X}_1)(\text{X}_2)\text{X}_3$, $-(\text{CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-OH}$, $-(\text{CH}_2)_n\text{-O-alkyl}$, $-(\text{CH}_2)_n\text{-O-alkenyl}$, $-(\text{CH}_2)_n\text{-O-alkynyl}$, $-(\text{CH}_2)_n\text{-O-(CH}_2)_m\text{-R}_7$, $-(\text{CH}_2)_n\text{-SH}$, $-(\text{CH}_2)_n\text{-S-alkyl}$, $-(\text{CH}_2)_n\text{-S-alkenyl}$, $-(\text{CH}_2)_n\text{-S-alkynyl}$, $-(\text{CH}_2)_n\text{-S-(CH}_2)_m\text{-R}_7$, $-\text{C}(\text{O})\text{C}(\text{O})\text{NH}_2$, or $-\text{C}(\text{O})\text{C}(\text{O})\text{OR}'_7$;

R_7 represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R'_7 represents, for each occurrence, hydrogen, or a substituted or unsubstituted alkyl, alkenyl, aryl, aralkyl, cycloalkyl, cycloalkenyl or heterocyclyl;

R_{32} is a small hydrophobic group;

R_{30} represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group or



R_{50} represents O or S;

R_{51} represents N_3 , SH, NH_2 , NO_2 or OR'_7 ;

R_{52} represents hydrogen, a lower alkyl, an amine, OR'_7 , or a pharmaceutically acceptable salt, or

R_{51} and R_{52} taken together with the phosphorous atom to which they are attached complete a heterocyclic ring having from 5 to 8 atoms in the ring structure;

X_1 represents a halogen;

X_2 and X_3 each represent a hydrogen or a halogen;

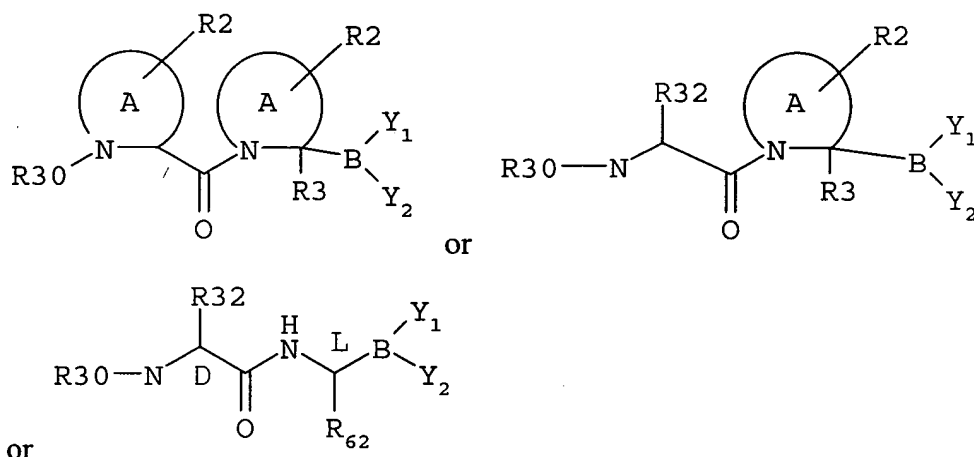
m is zero or an integer in the range of 1 to 8; and

n is an integer in the range of 1 to 8.

28-29. (Cancelled)

30. (Currently amended) A method for ~~modifying glucose metabolism of an animal~~ treating Type II diabetes in an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and or (D)-Ala-(L)-Ala in an amount sufficient to treat the Type II diabetes, but not sufficient to suppress the immune system of the animal.

31. (Previously presented) The method of claim 30, wherein the boronyl peptidomimetic is represented in the general formula:



or

wherein

each A independently represents a 4-8 membered heterocycle including the N and a C α carbon;

R₂ is absent or represents one or more substitutions to the ring A, each of which can

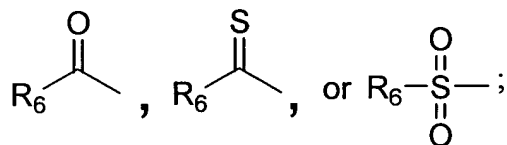
independently be a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₇, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-(CH₂)_m-R₇, -(CH₂)_m-SH, -(CH₂)_m-S-lower alkyl, -(CH₂)_m-S-lower alkenyl, or -(CH₂)_n-S-(CH₂)_m-R₇;

R₃ represents hydrogen or a halogen, a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl, a thiocarbonyl, an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -lower alkyl, $-(CH_2)_m-O$ -lower alkenyl, $-(CH_2)_n-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -lower alkyl, $-(CH_2)_m-S$ -lower alkenyl, or $-(CH_2)_n-S-(CH_2)_m-R_7$;

R₆ represents hydrogen, a halogen, an alkyl, an alkenyl, an alkynyl, an aryl, $-(CH_2)_m-R_7$, $-(CH_2)_m-OH$, $-(CH_2)_m-O$ -alkyl, $-(CH_2)_m-O$ -alkenyl, $-(CH_2)_m-O$ -alkynyl, $-(CH_2)_m-O-(CH_2)_m-R_7$, $-(CH_2)_m-SH$, $-(CH_2)_m-S$ -alkyl, $-(CH_2)_m-S$ -alkenyl, $-(CH_2)_m-S$ -alkynyl, or $-(CH_2)_m-S-(CH_2)_m-R_7$;

R₇ represents, for each occurrence, a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle;

R₃₀ represents a C-terminally linked amino acid residue or amino acid analog, or a C-terminally linked peptide or peptide analog, or an amino-protecting group, or



R₃₂ and R₆₂, independently, represent small hydrophobic groups;

Y₁ and Y₂ can independently or together be OH, or a group capable of being hydrolyzed to a hydroxyl group, or cyclic derivatives where Y₁ and Y₂ are connected via a ring having from 5 to 8 atoms in the ring structure;

m is zero or an integer in the range of 1 to 8; and n is an integer in the range of 1 to 8.

32. (Previously presented) The method of claim 31, wherein administering the boronyl peptidomimetic reduces one or more of insulin resistance, glucose intolerance, hyperglycemia, hyperinsulinemia, obesity, hyperlipidemia, or hyperlipoproteinemia.

33. (Previously presented) The method of claim 31, wherein the boronyl peptidomimetic has an EC₅₀ for modification of glucose metabolism which is at least one order of magnitude less than its EC₅₀ for immunosuppression.

34. (Previously presented) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for inhibition of glucose tolerance in the nanomolar or less range.
35. (Previously presented) The method of claim 31, wherein the boronyl peptidomimetic has an EC_{50} for immunosuppression in the μM or greater range.
36. (Previously presented) The method of claim 31, wherein the boronyl peptidomimetic is administered orally.
37. (Cancelled)
38. (Cancelled)
39. (Previously presented) The method of claim 14, wherein the inhibitor is administered in a single dosage.
40. (Previously presented) The method of claim 39, wherein the total daily dosage of the inhibitor is less than 2000 mg.